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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,641	10/27/2003	Deanna L. Kroetz	UCDVP018C2US/2000-094-3	4011

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EXAMINER	
FINN, MEGHAN R	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
12/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO@wavsip.com

Office Action Summary	Application No.	Applicant(s)	
	10/694,641	KROETZ ET AL.	
	Examiner	Art Unit	
	MEGHAN FINN	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on August 20, 2010 has been entered.

Applicants' arguments, filed August 20, 2010 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 54-60, 62-70, and 72-74 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 49-50 and 52 U.S. Patent No. 7,662,910. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both claim methods of treating hypertension or reducing blood pressure or the patient has renal disease with the same compounds. The compounds of claim 1 in 7,662,910 are broader than applicant's claimed range, however they encompass applicant's claimed compounds and examples

of compounds of formula 1 that read upon the claimed compounds are in claims 18-29 (of patent 7,662,910). Both the instant application and patent 7,662,910 both claim the same compounds to treat hypertension thus they are both claiming the same subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has amended the claims to add new claims 58-60, which depend from claim 54 which is a general method of treating hypertension in a patient with compounds of a generic formula. In claims 58-60, applicant specifies that the patient has "high normal blood pressure" (claim 58), is at risk for cardiovascular disease or renal disease (claim 59) or has cardiovascular or renal disease (claim 60). These amendments present new matter as there is no support for them in the originally filed disclosure. Applicant does identify hypertension as a risk factor for cardiovascular disease so does have written support for a patient at risk for cardiovascular disease but

not renal disease. Applicant never discloses treating patient with cardiovascular or renal disease and applicant never discloses a patient with "high normal blood pressure" and thus it does not appear to one of skill in the art that applicant has written support for such a patient. Thus claims 58-60 lack written description of the invention.

Claims 54-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of hypertension with N,N'-dicyclohexylurea (also known as DCU, see specification page 28, lines 25-30) , does not reasonably provide enablement for treatment of hypertension with other compounds from the formulas of claim 54, 64, and 74. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicant claims a method of treating hypertension with compounds of a very generic formula in claim 54. The compounds encompassed by this formula vary widely, and while applicant has added additional limitations to specify what groups can be substituted in R1 and R3 they still encompass thousands of possible structures that can vary significantly from each other. Even just looking at the compounds of Table 1 (pages 3-13 of specification) there is a great deal of variation. Applicant has only tested one compound, DCU for activity and it is a simple compound where both R1 and R3 are cyclohexyl groups. Applicant has not shown how to make any of the compounds of their invention, and while some compounds may be known in the art for purposes other than treating hypertension, many of the compounds encompassed by the claims are not well

known in the art and their synthesis would not be easily determined. DCU and the synthesis of DCU is known in the art, so applicant does not need to show how to make that compound however other compounds which are not known have no direction or examples to allow one of skill in the art to make the compounds. Further, applicant has not provided any direction that would lead one of skill in the art to believe that all of these compounds which vary significantly from DCU would have the same activity. Zanger et al. (Remington's Pharmaceutical Sciences, Chapter 27) teaches that structural formulas are not predictive of the physical, chemical, or biologic properties of a molecule. That drugs which are strikingly similar in structure can exhibit widely differing pharmacologic properties (page 425, column 1, paragraph 1). One of skill in the art cannot expect based solely on structures drawn, especially when those vary so much in structure from one species to another to have the same or similar activity and applicant's claims are not directed to compounds, they are drawn to a method of treating patients and thus to enable the claims one of skill in the art needs to be able to use these compounds to treat hypertension without undue experimentation to find out which compounds might have this activity. Thus one of skill in the art would not be able to make or use the invention as claimed.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2)

the amount of direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The amount of experimentation would be undue (1) because there is no direction or working examples beyond the compound DCU which is not representative of the generic structure and varies significantly from many of the compounds (2,3). The nature of the invention is treatment of hypertension with a wide variety of compounds which would be expected by one of skill in the art to have quite a range of different activities (4) and the state of the prior art is such that many of the most complex compounds of the generic claims are not known in the art and thus neither their activity or synthesis is known (5). The relative skill of those in the art is high (6), however the unpredictability of using compounds that have not been shown to have any activity to treat a human patient with a specific desired result is very high (7) and the breadth of the claims is large due to the large number of compounds encompassed by the claims generic formula (8).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 58 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 58 applicant claims the patient of claim 54 has "high normal blood pressure". It is unclear how a patient can have high blood pressure and normal blood pressure at the same. Or is it on the high end of a normal range? Or is the high blood pressure normal for that patient? What is Normal? The concept of normal varies greatly from one person of skill in the art to the next and while most would agree that a blood pressure of say 180/100 is high blood pressure it is less clear what one of skill in the art would consider is the range of blood pressures a patient could have and still be considered a patient who has "high normal blood pressure". Thus claim 58 is rejected for failing to point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 54, 56-60, 62-64, 66-70, 72-74 are rejected under 35 U.S.C. 102(b) as being anticipated by Archibald et al. (Antihypertensive Ureidopiperidines, 1980, J. Med. Chem.).

In claims 54, 64, and 74 applicant claims a method of reducing blood pressure in a patient comprising administering a compound of a generic formula. Archibald et al.

teaches their compounds as antihypertensive agents and tested the effects at lowering blood pressure in rats. Many of the compounds read upon applicants claims. For claim 54, applicant claims R1 or R3 is selected from a heterocyclic compound and then applicant further specifies substituents but only specifies those for heteroaryls, not heterocyclic compounds and thus the compounds number 1-11, 16, 21-32, 39-42, 44-52, and 59-64 of Archibald et al. read upon claim 54 (see table I on pages 858-859). Claims 64 and 74 are slightly more narrow requiring that at least one R group is a cycloalkyl or alkyl (claim 64) or that if one R is an aryl that the other R is not a heteroaryl or aryl. Since all of the compounds of Archibald et al. have a heterocyclic compound but not a heteroaryl compounds number 1-11, 16, 21-32, 39-42, 44-52, and 59-64 of Archibald et al. also read upon claim 74. For Claim 64, at least one group must be an alkyl or cycloalkyl and thus compounds No 10-11 read upon claim 64. Archibald et al. reported activity of these compounds and many of the compounds that read upon applicants claims had activity in reducing blood pressure including for example compounds 10-11 (page 860, table II). Compounds 10 and 11 of Archibald et al. read upon all of the independent claims. Thus these compounds lowered blood pressure in a patient and Archibald et al. anticipates claims 54, 64, and 74.

In claims 56-59 and 66-69, applicant claims that the patient has hypertension (claims 56 and 66), or that the method results in a reduction of systolic blood pressure (claim 57 and 67) or is at risk for cardiovascular disease (claims 69 and 69). The rats of Archibald et al. have high blood pressures starting in ranges 160-200mmHg (page 860, table II notes) and are thus patients with hypertension and table II shows a reduction in

systolic blood pressure. Hypertension is a risk factor for cardiovascular disease as acknowledged by applicant in the background information of their specification (page 1, [0004]) and thus those patients are at risk for cardiovascular disease. Thus claims 56-59 and 66-69 are anticipated by Archibald et al. for the reasons discussed above.

In claims 60 and 70, applicant claims that the patient has cardiovascular disease or renal disease. Archibald et al. tested their compounds on renal hypertensive rats (page 857, column 1) and thus the patients of Archibald et al. had renal disease and claims 60 and 70 are anticipated by Archibald et al.

In claims 62-63 and 71-72, applicant claims that the inhibitor of claims 54 or 64 inhibits soluble epoxide hydrolase with a specific IC50 value. These values are results of the methods of claim 54 and thus the methods of Archibald et al. must necessarily result in those values because they administer the same compounds to the same patients. Thus claims 64-63 and 71-72 are anticipated by Archibald et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 54, 55-60, 62-70 and 72-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Archibald et al. (Antihypertensive Ureidopiperidines, 1980, J. Med. Chem.).

Claims 54, 56-60, 62-64, 66-70 and 72-74 are anticipated by Archibald et al. as discussed above. Archibald et al. teaches each and every limitation of those claims, and thus also renders the claims obvious. It would have been clear to one of ordinary skill in the art at the time of the invention that Archibald et al. teaches their compositions for treatment of hypertension, including renal hypertension because the rats tested had renal hypertension.

In claims 55 and 65, applicant claims the patient is a human. Archibald et al. tested their compounds on rats, however it would have been obvious to one of ordinary skill in the art at the time of the invention that the compound are meant to be used to treat humans with hypertension and are being tested on rats for convenience and safety reasons. Thus it would be obvious to use the antihypertensive agents to treat humans and claims 55 and 65 are unpatentable over Archibald et al.

Claims 54, 56-64 and 66-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Archibald et al. (Antihypertensive Ureidopiperidines, 1980, J. Med. Chem.), in further view of Zuckerman et al. (US 5,447,941).

Claims 61 and 71 depend on claims 54 and 64 respectively and those claims as well as claims 56-60, 60-64, 66-70 and 72-74 are obvious over Archibald et al. as discussed above the reasons of which are herein incorporated by reference. In claims 61 and 71, applicant further claims the inhibitor is administered orally. Archibald et al. does not say how their compounds were administered. Zuckerman et al. teaches compound for treating pulmonary hypertension (abstract) and teaches that the compounds can be formulated as tablets or elixirs for convenient oral administration (column 2, line 67 to Column 3 line 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to use oral administration for convenience when treating humans with the compounds of Archibald et al. and thus claims 60 and 70 are unpatentable over Archibald et al.

Conclusion

No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 7:30am-5pm Mon-Thu, 7:30am-4pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/Leslie A. Royds/
Primary Examiner, Art Unit 1614